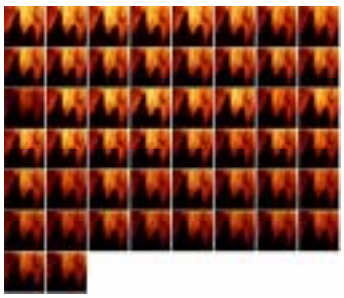
# 3D Molecular Bioimaging Mass Spectrometry

*Three dimensional (3D) molecular imaging SIMS is achieved by acquiring a series of characteristic molecular secondary ion images as a function of increasing depth during dynamic SIMS sputtering of thin molecular films using cluster primary ion bombardment. Reconstruction of the resulting image stack provides a 3D volumetric image of the molecular composition of the sample. NIST researchers have used this approach to examine several different types of samples including thin polymer films, multilayer polymer films, polymer films doped with pharmaceuticals and biological thin sections.*

**G. Gillen, C. Szakal, A. Fahey, and C. Mahoney (Div. 837)**

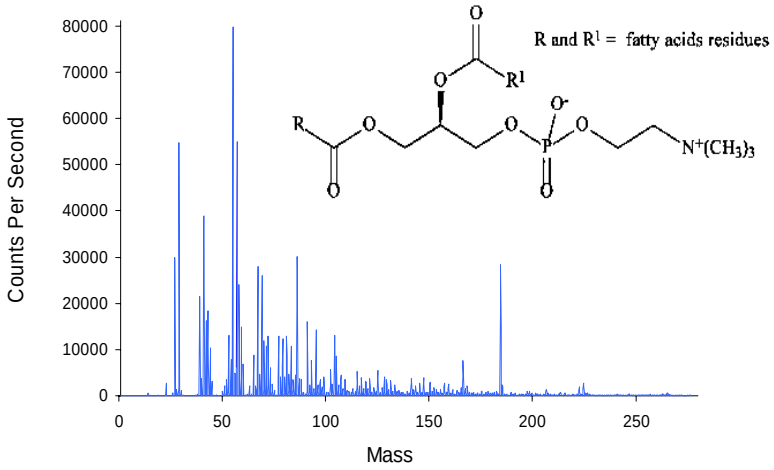
In recent years, the use of cluster primary ion projectiles for organic secondary ion mass spectrometry (SIMS) has generated considerable interest as a method to improve molecular secondary ion yields, facilitate improved sensitivity for large molecule analysis and minimize the accumulation of beam-induced damage in selected organic materials. In this work, we report on our attempts to combine $SF_5^+$ primary ion bombardment with secondary ion imaging on an ion microscope SIMS instrument to produce spatially resolved molecular information as a function of depth.

## 3D SIMS images have been obtained on the NIST ion microscope SIMS instrument using an $SF_5^+$ primary ion beam.



Microscope imaging is particularly suited for use with cluster ion beam sources because the requirement for a highly focused primary ion beam is eliminated. This allows large diameter, higher current and lower impact energy cluster ion beams to be used which in turn allows for higher sputtering rates, faster analysis times and increased depth resolution. Image acquisition rates can be further increased since the secondary ion signal from each pixel in the image is acquired and digitized in parallel. An example of microscope-based molecular image depth profiling is shown in the graphic for a 5 micrometer thick rat brain section on silicon.

***The SIMS mass spectrum of rat brain section shows the high yield of the characteristic parent ion at m/z 184 for phosphotidylcholine. Secondary ion image stack of the phosphotidylcholine molecular ion distribution as a function of time through a 5 micrometer thick rat brain section is shown in the graphic. Each image acquisition was 10 seconds with a 500 micrometer field-of-view.***




In this example we show the cluster SIMS mass spectrum for the tissue section which demonstrates a high signal for the m/z 184 phosphatidylcholine molecular ion.

Phosphatidylcholine is a phospholipid that is a major constituent of brain tissue. The distribution of this compound was mapped by acquiring a series of images as a function of increased sputter time into the tissue sample. No degradation in molecular ion signal was observed during the analysis. In this example, the phosphotidylcholine was non uniformly distributed as a function of depth and was anti-correlated with the cholesterol molecular ion distribution (data not shown).

***Future Plans:*** $SF_5^+$ molecular image depth profiling has been demonstrated for a series of polymer films, polymer bilayers, patterned polymer films, polymers containing organic molecules and biological tissues. We plan to extend this work to study imaging of biomarkers within individual cancer cells grown from culture for early cancer detection. This capability will be enhanced by the addition of a $C_{60}$ cluster ion source for molecular depth profiling of biological tissue samples.